

Figure 1

BEST AVAILABLE COPY

HK 5 / MF AVHLM AFYFSK LK - - EDQIK EVD RFL YH M 29
 HK1 / MI AAQ LLA YFTE LK - - DDQVK EID K YL YAM 29
 HK2 / MI ASH LLA YFTE LN - - HDQVQ EVD Q YL YH M 29
 HK3 / MDSIGSSGLRQ GEETLSCSEEG L PGP S DSSELVQEC LQQF 40
 HK4p / 0

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|-------|----|---|---|----|
| HK 5 | 30 | R L S D D T I L D I M R | R F F R A E M E K G L A K D T N P T A A V K M L P T F V R | 69 |
| HK 1 | 30 | R L S D E I L I D I M T | R F F R K E M E K N G L S R D F N P T A T V K M L P T F V R | 69 |
| HK 2 | 30 | R L S D E I L L E I S K | R F F R K E M E K G L G A T T H P T A A V K M L P T F V R | 69 |
| HK 3 | 41 | K V I R A Q L Q Q I Q A S L L G S M E Q A L R G Q A S P A P A V R M L P T Y V G | 80 | |
| HK 4p | 1 | | | 0 |

HK 5 70 A I P D G S E N G E F L S L D L G G S - K F R V L K V Q V A E E G K R H V Q M 107
 HK 1 70 S I P D G S E K G D F I A L D L G G S - S F R I L R V Q V N H E K N Q N V H M 107
 HK 2 70 S T P D G I E H G E F L A L D L G G T - N F R V L W V K Y T D N G L Q K V E M 107
 HK 3 81 S T P H G I E Q G D F V V L E L G A T G A S L R V L W V T L T G I E G H R V E P 120
 HK 4p 1

HK 5 108 ES Q F Y P T P N E I I R G N G I E L F E Y V A D C L A D F M K T K D L E H K K 147
HK 1 108 E S E V Y D T P E N I V H G S G S Q L F D H V A E C L G D F M E K R K I E D K K 147
HK 2 108 E N Q I Y A I P E D I M R G S G T Q L F D H I A E C L A N F M D K L Q I E D K K 147
HK 3 121 R S Q E F V I P Q E V M L G A G Q Q L F D F A A H C L S E F L D A Q P V N K Q G 160
HK 4p 1

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|--------------|-----|---|---|-----|
| <i>HK 5</i> | 148 | L P L G L I F S F P C R Q T K L E E | G V L L S W I K K F K A R G V Q D T D V V S | 187 |
| <i>HK 1</i> | 148 | L P V G F I F S F P C Q Q S K I D E A I L I T W I K R F K A S G V E G A D V V K | | 187 |
| <i>HK 2</i> | 148 | L P L G F I F S F P C H Q T K L D E S F L V S W I K G F K S S G V E G R D V V A | | 187 |
| <i>HK 3</i> | 161 | L Q L G F S F S F P C H Q T I G L D R S T L I S W I K G F R C S G V E G Q D V V Q | | 200 |
| <i>HK 4p</i> | 1 | | | 0 |

HK5 188 R L T K A M R R E H K D M D V D I L A L V N D I V G I M M T C A Y D D P Y C E V G 227
 HK1 188 L L N K A I K K R G D Y D A N I V A V V N D I V G I M M T C G Y D D Q H C E V G 227
 HK2 188 L I R K A I Q R R G D F D I D I V A V V N D I V G I M M T C G Y D D H N C E I G 227
 HK3 201 L L R D A I R R Q G A Y N I D V V A V V N D I V G I M M G C E P G V R P C E V G 240
 HK4p 1

Figure 2a

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|-------|-----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-----|
| HK 5 | 228 | V | I | I | G | T | G | T | N | A | C | Y | M | E | D | M | S | N | I | D | L | V | E | G | D | E | G | R | M | C | I | N | T | E | V | G | A | F | G | D | 267 |
| HK 1 | 228 | L | I | I | G | T | G | T | N | A | C | Y | M | E | E | L | R | H | I | D | L | V | E | G | D | E | G | R | M | C | I | N | T | E | V | G | A | F | G | D | 267 |
| HK 2 | 228 | L | I | V | G | T | G | S | N | A | C | Y | M | E | E | M | R | H | I | D | M | V | E | G | D | E | G | R | M | C | I | N | M | E | V | G | A | F | G | D | 267 |
| HK 3 | 241 | L | V | V | D | I | G | T | N | A | C | Y | M | E | E | A | R | H | V | A | V | L | D | E | D | R | G | R | V | C | V | S | V | E | V | G | S | L | S | D | 286 |
| HK 4p | 1 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | 0 | | | | | | | | | | | |

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| HK 5 | 268 | G | A | L | E | D | I | R | T | E | F | D | R | E | L | D | L | G | S | L | N | P | G | K | Q | L | F | E | K | M | I | S | G | L | Y | L | G | E | L | V | R | 307 |
| HK 1 | 268 | G | S | L | E | D | I | R | T | E | F | D | R | E | I | D | R | G | S | L | N | P | G | K | Q | L | F | E | K | M | I | S | G | M | Y | L | G | E | L | V | R | 307 |
| HK 2 | 268 | G | S | L | N | D | I | R | T | E | F | D | Q | E | I | D | M | G | S | L | N | P | G | K | Q | L | F | E | K | M | I | S | G | M | Y | M | G | E | L | V | R | 307 |
| HK 3 | 281 | G | A | L | G | P | V | L | T | T | F | D | H | T | L | D | H | E | S | L | N | P | G | A | Q | R | F | E | K | M | I | G | G | L | Y | L | G | E | L | V | R | 320 |
| HK 4p | 1 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | 0 | | | | | | | | | | | | |

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| HK 5 | 308 | L | I | L | K | M | A | K | A | G | L | F | G | G | E | K | S | S | A | L | H | T | K | G | K | I | E | T | R | H | V | A | A | M | E | K | Y | K | E | 347 | | |
| HK 1 | 308 | L | I | L | V | K | M | A | K | E | G | L | F | E | G | R | I | T | P | E | L | L | T | R | G | K | F | N | T | S | D | V | S | A | I | E | K | N | K | E | 347 | |
| HK 2 | 308 | L | I | L | V | K | M | A | K | E | E | L | F | G | G | K | L | S | P | E | L | L | N | T | G | R | F | E | T | K | D | I | S | D | I | E | G | E | K | D | 347 | |
| HK 3 | 321 | L | V | L | A | H | L | A | R | C | G | V | L | F | G | G | C | T | S | P | A | L | L | S | Q | G | S | I | L | L | E | H | V | A | E | M | E | D | P | S | T | 366 |
| HK 4p | 1 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | 0 | | | | | | | | | | | | |

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| HK 5 | 348 | G | L | A | N | T | R | E | I | L | V | D | L | G | L | E | P | S | E | A | D | C | I | A | V | Q | H | V | C | T | I | V | S | F | R | S | A | N | L | C | A | 387 |
| HK 1 | 348 | G | L | H | N | A | K | E | I | L | T | R | L | G | V | E | P | S | D | D | C | V | S | V | Q | H | V | C | T | I | V | S | F | R | S | A | N | L | V | A | 387 | |
| HK 2 | 348 | G | I | R | K | A | R | E | V | L | M | R | L | G | L | D | P | T | Q | E | D | C | V | A | T | H | R | I | C | Q | I | V | S | T | R | S | A | S | L | C | A | 387 |
| HK 3 | 361 | G | A | A | R | V | H | A | I | L | Q | D | L | G | L | S | P | G | A | S | D | V | E | L | V | Q | H | V | C | A | A | V | C | T | R | A | A | Q | L | C | A | 406 |
| HK 4p | 1 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | 0 | | | | | | | | | | | | |

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| HK 5 | 388 | A | A | L | A | A | I | L | T | R | L | R | E | N | K | K | V | E | R | L | R | T | T | V | G | M | D | G | T | L | Y | K | I | H | P | Q | Y | P | K | R | L | 427 |
| HK 1 | 388 | A | T | L | G | A | I | L | N | R | L | R | D | N | K | G | T | P | R | L | R | T | T | V | G | V | D | G | S | L | Y | K | I | H | P | Q | Y | S | R | R | F | 427 |
| HK 2 | 388 | A | T | L | A | A | V | L | Q | R | I | K | E | N | K | G | E | E | R | L | R | S | T | I | G | V | D | G | S | V | Y | K | H | P | H | F | A | K | R | L | 427 | |
| HK 3 | 401 | A | A | L | A | A | V | L | S | C | L | Q | H | S | R | E | Q | Q | T | L | Q | V | A | V | A | T | G | G | R | V | C | E | R | H | P | R | F | C | S | V | L | 446 |
| HK 4p | 1 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | 0 | | | | | | | | | | | | |

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| HK 5 | 428 | H | K | V | V | R | K | L | V | P | S | C | D | V | R | F | L | L | S | E | S | G | S | T | K | G | A | A | M | V | I | A | V | A | S | R | V | Q | A | Q | R | 467 | |
| HK 1 | 428 | H | K | T | L | R | R | L | V | P | D | S | D | V | R | F | L | L | S | E | S | G | S | G | K | G | A | A | M | V | I | A | V | A | Y | R | L | A | E | Q | H | 467 | |
| HK 2 | 428 | H | K | I | V | R | R | L | V | P | G | C | D | V | R | F | L | R | S | E | D | G | S | G | K | G | A | A | M | V | I | A | V | A | Y | R | L | A | D | Q | H | 467 | |
| HK 3 | 441 | Q | G | T | V | M | L | L | A | P | E | C | D | V | S | L | I | P | S | V | D | G | G | R | G | V | A | M | V | I | A | V | A | A | R | L | A | A | H | R | 486 | | |
| HK 4p | 1 | | | | | | | | | | | | | | | | | | | | | | | | | | | | | 0 | | | | | | | | | | | | | |
| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | | M | L | D | D | R | A | R | M | E | A | A | K | K | 12 |

Figure 2b

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| | | | |
|------|-----|---|-----|
| HK 5 | 468 | KQIDRVIALFQLTREQLVDPVQAKMRAELEYGLEKKSHGLA | 507 |
| HK1 | 468 | RQIEETLAHFHLTKDMLLEVKKRMRAEMELGLRKQTHNNA | 507 |
| HK2 | 468 | RARQKILEHLQLSHDQLLEVKKRMKVEMERGLSKEITHASA | 507 |
| HK3 | 481 | RLLEEILAPFRLNHDQLAAVQAQMRKAMAKGLRG - - EAS | 517 |
| HK4p | 14 | EKVEQILAEFQLQEDLKKVMRRMQKEMDRGLRL ETHEEA | 53 |
| HK 5 | 508 | TVRMLPTIYVCGLPDGTEK GKFLALDLGGTNFRVLLVKIERS | 547 |
| HK1 | 508 | VVKMLPSFVVRTIPDGTE NGDFLALDLGGTNFRVLLVKIERS | 547 |
| HK2 | 508 | PVKMLPTIYVCATPDGTEKGDFLALDLGGTNFRVLLVVRVN | 547 |
| HK3 | 518 | SLRMLPTIFVRAIPDGSEERGDFLALDLGGTNFRVLLVVRTI | 557 |
| HK4p | 54 | SVKMLPTIYVRSIPEGSEVGDFLSLDLGGTNFRVMLLVKVG | 57 |
| HK 5 | 548 | GR - R - - SVRMYNKFIFAIPLEIMQGTGEELFDHIVQCIADDF | 584 |
| HK1 | 548 | GKKR - - TVEMHNKIYAIPLEIMQGTGEELFDHIVSCISDF | 585 |
| HK2 | 548 | GKVG - - GVEMHNKIYAIPQEVMHGIGDELFDHIVQCIADDF | 585 |
| HK3 | 558 | G - - - - VQITSEIYSIPEITVAQGGGQQLFHDHIVDCIYDF | 591 |
| HK4p | 94 | GE EGQW SVKTEHQMYSIPE DAMTGTAEMLFDYIS E C IS DF | 123 |
| HK 5 | 625 | LDYMGLEGA SLPLGFTFSFPCQMSIDKGT LIGVTKGFKA | 624 |
| HK1 | 625 | LDYMGIKGPRMPLGFTFSFPCQQTSLDAGILITVTKGFKA | 625 |
| HK2 | 625 | LEYMGMEKVSLPLGFTFSFPCQQNSLDESILLKVTGFKFA | 625 |
| HK3 | 622 | QQKQGILSGQSLPLGFTFSFPCQQLGLDQGILLNVTKGFKA | 621 |
| HK4p | 124 | LDKHQM KHKLPLGFTFSFPRHEDIDKGILLNVTKGFKA | 173 |
| HK 5 | 625 | IDCEGE DVVDM LREAIKRRN EFDLDIVAVVNDIVGTMMTC | 664 |
| HK1 | 626 | IDC VGH DVVILLRD AIKRRE EFDLDVVAVVNDIVGTMMTC | 665 |
| HK2 | 626 | SGCEGE DVVILLKEAIHRRRE EFDLDVVAVVNDIVGTMMTC | 665 |
| HK3 | 632 | SDCEGQ DVVSLLEAI TTRQAVELNVVAIVNDIVGTMMSC | 671 |
| HK4p | 174 | SGAEGNN VVG LLRDAIKRRG DFE MDVVA M VNDIVATMISC | 213 |
| HK 5 | 665 | GYEDPN CEIGLIAGTGSNM CYMEDMRN IEM VEGGE GEMCI | 704 |
| HK1 | 666 | AYEEPT CEVGLIVGTGSNACYMEEMKNVEM VEGDQGQMC I | 705 |
| HK2 | 666 | GFEDPH CEVGLIVGTGSNACYMEEMRNVEL VEGEEGRMCV | 705 |
| HK3 | 672 | GYEDPR CEIGLIVGTGTINACYMEE LRNVAGVP GDSGRMC I | 711 |
| HK4p | 214 | YTEDHQ CEVGMIVGTGC NACYMEEMQ NVEL VEGDEGRMCV | 253 |

Figure 2c

HK 5 705 NT EWG GFGDNGC I D D I R T R Y D T E V D E G S L N P G K Q R Y E K M T 744
 HK 1 706 NMEVGAFGDNGCLDD I R T H Y D R L V N E Y S L N A G K Q R Y E K M I 745
 HK 2 706 NMEVGAFGDNGCLDD F R T E F D V A V D E L S L N P G K Q R F E K M I 745
 HK 3 712 NMEVGAFGD D G S L A M L S T R F D A S V D Q A S I N P G K Q R F E K M I 751
 HK 4p 254 NT EWGAFGD S G E L D E F L L E Y D R L V D E S S A N P G Q Q L Y E K L I 293

HK 5 745 S G M Y L G E I V R Q I L I D L T K Q G L L F R G Q I S E R L R T R G I F E T K 784
 HK 1 746 S G M Y L G E I V R N I L I D F T K K G F L F R G Q I S E T M K T R G I F E T K 785
 HK 2 746 S G M Y L G E I V R N I L I D F T K R G L L F R G R I S E R L K T R G I F E T K 785
 HK 3 752 S G M Y L G E I V R H I L L H L T S L G V L F R G Q Q I Q R L Q T R D I F K T K 791
 HK 4p 294 G G K Y M G E L V R L V L L R L V D E N L L F H G E A S E Q L R T R G A F E T R 333

HK 5 785 F L S Q I E S D R L A L L Q V R I L Q Q L G L D S T C E D S I V V K E V C G A 824
 HK 1 786 F L S Q I E S D R L A L L Q V R A I L Q Q L G L N S T C D D S I L V K T V C G V 825
 HK 2 786 F L S Q I E S D C L A L L Q V R A I L Q H L G L E S T C D D S I I V K E V C T V 825
 HK 3 792 F L S E I E S D S L A L R Q V R A I L E D L G L P L T S D D A L M V L E V C Q A 831
 HK 4p 334 F V S Q V E S D T G D R K Q I Y N I L S T L G L R P S T T D C D I V R R A C E S 373

HK 5 825 V S R R A A Q L C G A G L A A I V E K R R E D Q G L E H L R I T V G V D G I L Y 864
 HK 1 826 V S R R A A Q L C G A G M A A V V D K I R E N R G L D R L N V T V G V D G I L Y 865
 HK 2 826 V A R R A A Q L C G A G M A A V V D R I R E N R G L D A L K V T V G V D G I L Y 865
 HK 3 832 V S Q R A A Q L C G A G V A A V V E K I R G N R G L E E L A V S V G V D G I L Y 871
 HK 4p 374 V S T R A A H M C S A G L A G V I N R E M R E S E S E D V M R I T V G V D G S V Y 413

HK 5 865 K L H P H F S R I L Q E I V K E L A P R C D V I F M L S E D G S G K G A A L I T 904
 HK 1 866 K L H P H F S R I M H Q I V K E L S P K C N V S F L L S E D G S G K G A A L I T 905
 HK 2 866 K L H P H F A K V M H E I V K D L A P K C D V S F L Q S E D G S G K G A A L I T 905
 HK 3 872 K L H P R F S S L V A A I V R E L A P R C V V I F L Q S E D G S G K G A A L V I 911
 HK 4p 414 K L H P S F K E R F H A S V R R L T P S C E I T F I E S E E G S G R G A A L V S 453

HK 5 905 A V A K R L Q Q A Q K E N 917
 HK 1 906 A V G V R L R T E A S S 917
 HK 2 906 A V A C R I R E A G Q R 917
 HK 3 912 A V A C R L A Q L T R V 923
 HK 4p 454 A V A C K K A C M L G Q 465

Figure 2d

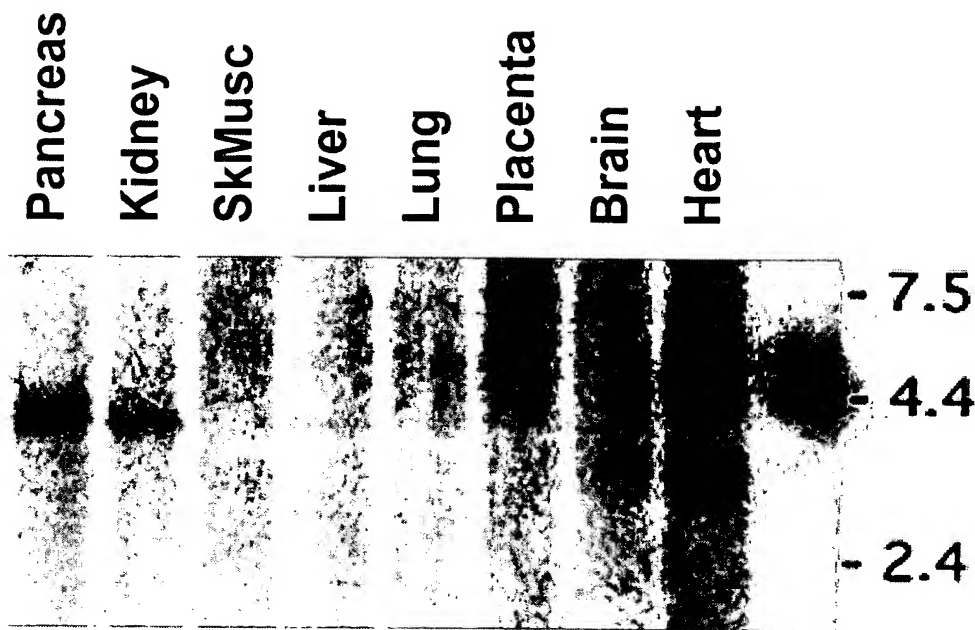


Figure 3

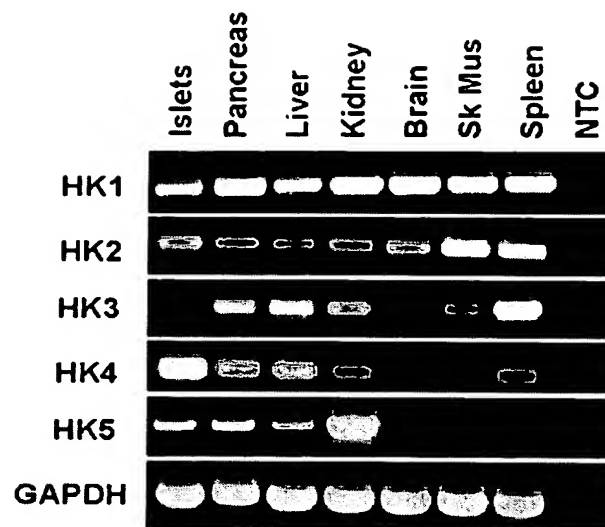


Figure 4

Figure 5



Insulin

HK5

merge

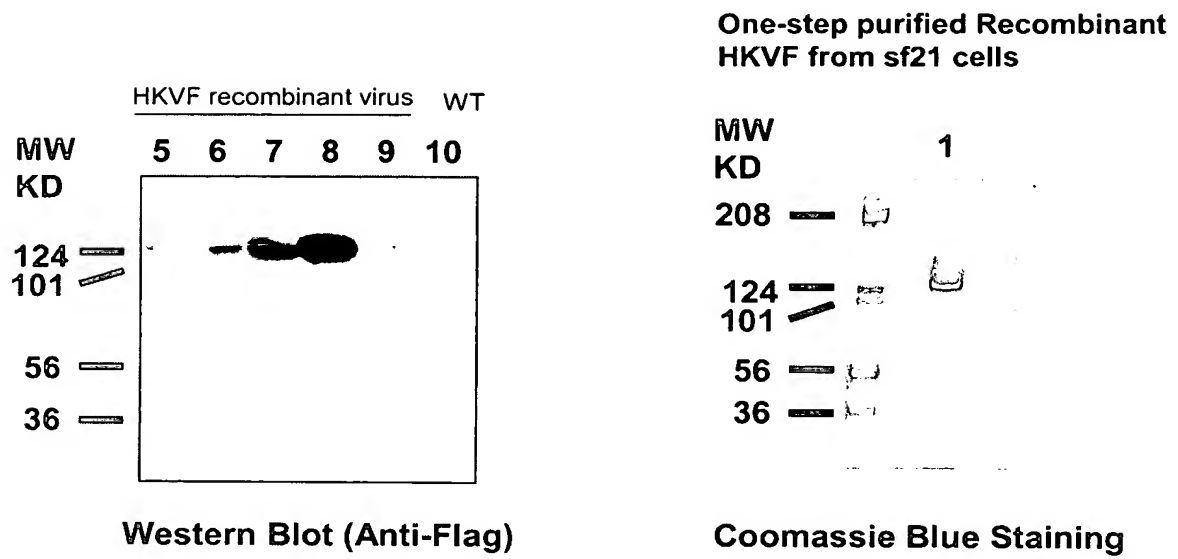


Figure 6a.

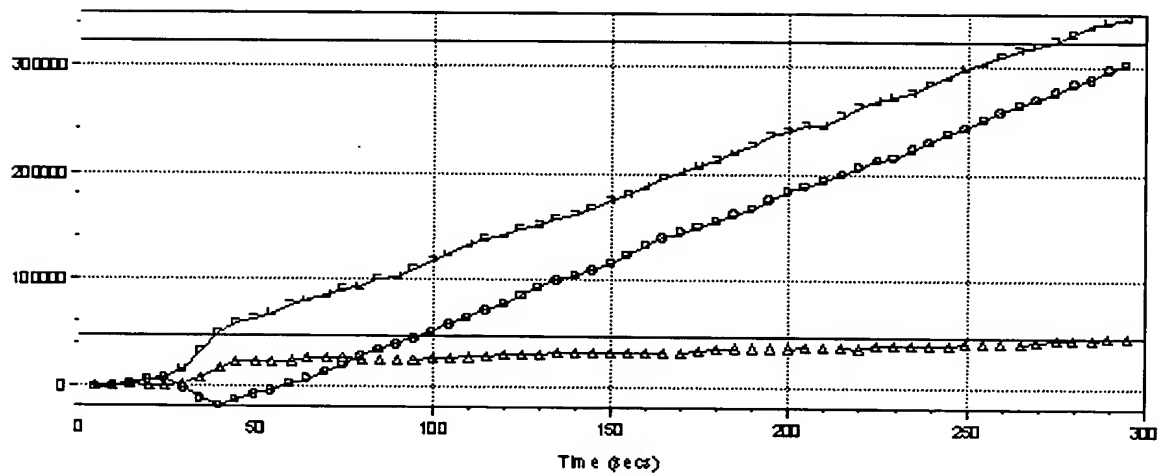
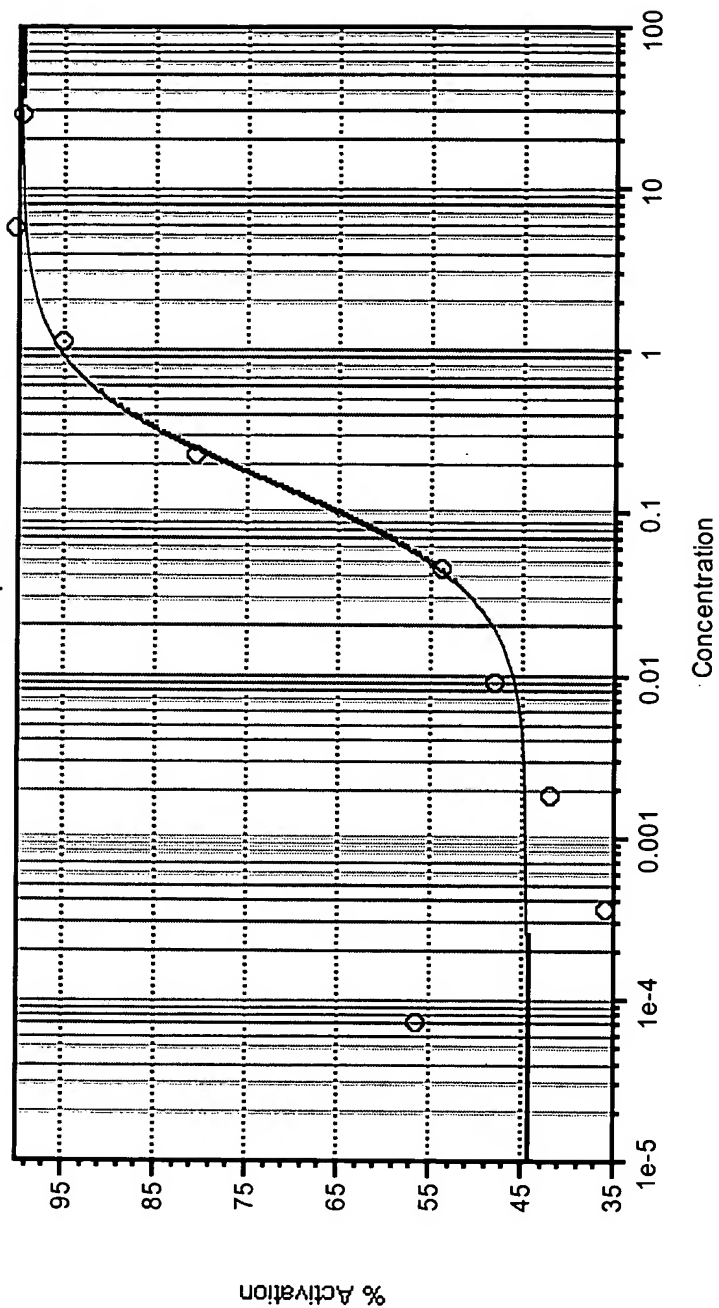


Figure 6 b

Graph#1



$y = (A - D) / (1 + (x/C)^B) + D$
 Plot#1 (Data: Concentration vs % Activation) \underline{A} 44.196 \underline{B} 1.296 \underline{C} 0.152 \underline{D} 99.518 $\underline{R^2}$ 0.961

Figure 7

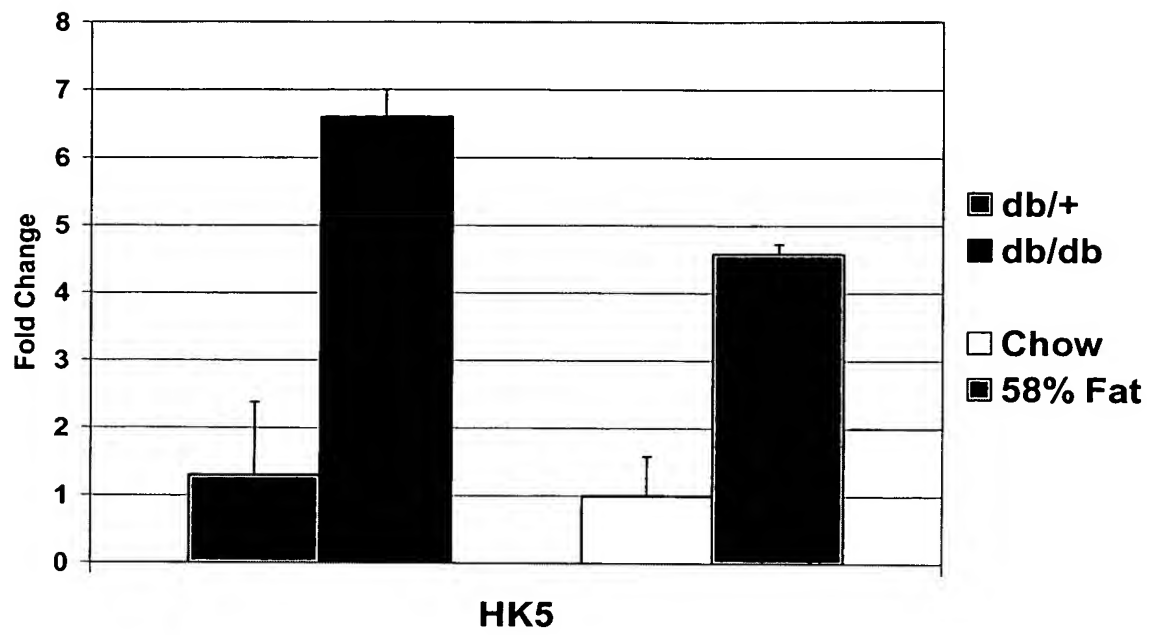
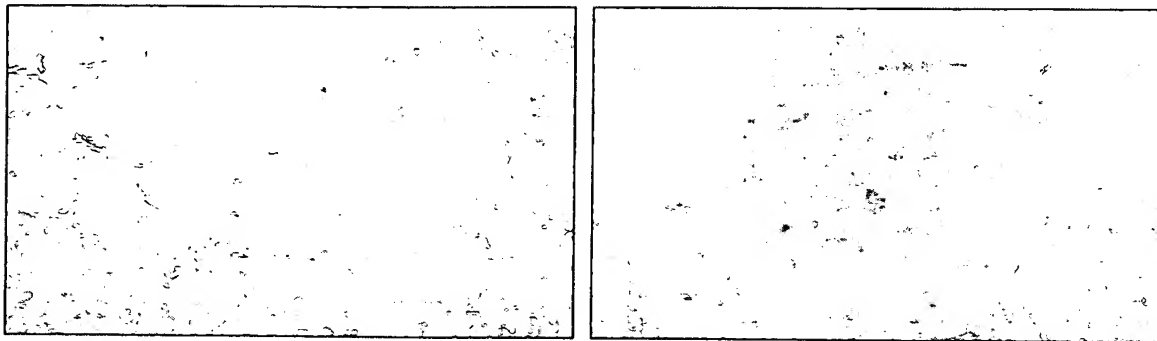


Figure 8



Db/+

Db/Db

Anti mouse HKV

Figure 9

Figure 10

